IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
WACO DIVISION

Ravgen, Inc., Plaintiff, v. Quest Diagnostics Incorporated, Defendant.	Civil Action No. _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Ravgen, Inc. ("Ravgen"), for its Complaint against Defendant Quest Diagnostics Incorporated ("Quest"), hereby alleges as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 7,727,720 (the "'720 Patent") and 7,332,277 (the "'277 Patent") (collectively the "Patents-in-Suit"), arising under the Patent Laws of the United States, 35 U.S.C. §§ 271 *et seq*.

THE PARTIES

2. Plaintiff Ravgen is a Delaware corporation with its principal place of business at 9241 Rumsey Rd., Columbia, MD 21045. Ravgen is a pioneering diagnostics company that focuses on non-invasive prenatal testing. Ravgen has spent millions of dollars researching and developing novel methods for the detection of cell-free DNA to replace conventional, invasive procedures. Ravgen's innovative cell-free DNA technology has various applications, including non-invasive prenatal and other genetic testing. Those efforts have resulted in the issuance of several patents, including the Patents-in-Suit.

3. Defendant Quest is a Delaware corporation with its principal place of business at 500 Plaza Drive, Secaucus, NJ 07094. (Ex. 6 at 1 (Texas Secretary of State certificate of fact and information letter for Quest Diagnostics Incorporated), Ex. 7 at cover (Quest Diagnostics Incorporated's Form 10-K for Fiscal Year 2019).) Quest is registered to do business in the state of Texas. (Ex. 6 at 2.) Quest has appointed Corporation Service Company (d/b/a CSC – Lawyers Incorporating Service Company), 211 E. 7th Street, Suite 620, Austin, TX 78701-3218 as its agent for service of process. (*Id.*) Quest maintains several places of business in this District, including patient collection centers that offer diagnostic tests (e.g., the QNatal Advanced test), such as at 3708 Jefferson Street, Suite B, Austin, TX 78731; and other offices, such as at 607 E. Sonterra Boulevard, Suite 306, San Antonio, TX 78258-4763. (*See, e.g.*, Ex. 8 at 1–2 (https://appointment.questdiagnostics.com/patient/findlocation); Ex. 9 (Dun & Bradstreet report for 3708 Jefferson Street location); Ex. 10 (Dun & Bradstreet report for 607 E. Sonterra Boulevard location); Ex. 11 (Google street view photos of 607 E. Sonterra Boulevard location).)

4. Quest commercializes genetic tests using cell-free DNA, including a non-invasive prenatal diagnostic test for the determination of fetal chromosomal abnormalities marketed under the trade name "QNatal Advanced." Quest offers and markets this test throughout the United States, at least through the website, www.questdiagnostics.com. (*See generally* Ex. 12 (https://www.questdiagnostics.com/home/patients/health-test-info/womens-health/prenatal/during-pregnancy/noninvasive/).)

JURISDICTION AND VENUE

5. Ravgen incorporates by reference paragraphs 1–4.

6. This action arises under the patent laws of the United States, including 35 U.S.C. §§ 271 *et seq*. The jurisdiction of this Court over the subject matter of this action is proper under 28 U.S.C. §§ 1331 and 1338(a).

7. Venue is proper in this District pursuant to U.S.C. §§ 1391(b), (c), (d), and 1400(b) because Quest has a permanent and continuous presence in, has committed acts of infringement in, and maintains regular and established places of businesses in this District.

8. By registering to conduct business in Texas and by having facilities where it regularly conducts business in this District, Quest has a permanent and continuous presence and regular and established places of business in the Western District of Texas.

9. Quest maintains regular and established places of business in this District, including at least patient collection centers that offer diagnostic tests (e.g., the QNatal Advanced test), such as at 3708 Jefferson Street, Suite B, Austin, TX 78731. (*See* Ex. 8 at 1–2; Ex. 9 (Dun & Bradstreet report identifying the business at this location as Quest Diagnostics Incorporated).) On information and belief, Quest holds out these places of business as Quest's own, including by displaying its name at these locations, listing these locations and directing patients to these locations on its website located at https://appointment.questdiagnostics.com/patient/findlocation. (*See* Ex. 8; Ex. 7 at 1 (Quest Diagnostics Incorporated's Form 10-K for Fiscal Year 2019) ("We conduct business through . . . our laboratories, patient service centers, offices and other facilities around the United States . . . ."); *id.* at 38 ("We also maintain offices . . . and patient service centers at locations throughout the United States.").) Further, Quest's places of business in this District include other offices, such as at 607 E. Sonterra Boulevard, Suite 306, San Antonio, TX 78258-4763. (*See* Ex. 10 (Dun & Bradstreet report identifying the business at this location as Quest Diagnostics Incorporated); Ex. 11 (Google street view photos of this location showing "Quest

Diagnostics").) On information and belief, employees of Quest carry out Quest's business at places of business in this District. (*See, e.g.*, Ex. 13 (https://careers.questdiagnostics.com/en-US/job/phlebotomist-ii-austin-tx-req51029/J3S63W6HHT6BY14S39T) (advertising Phlebotomist II job, responsible for "[c]ollect[ing] specimens according to established procedures," at 3708 Jefferson Street, Austin, TX); Ex. 14 (https://careers.questdiagnostics.com/en-US/job/patient-services-mgr-san-antonio-tx-req51346/J3N15778G37RWGTGH16) (advertising Patient Services Manager job at 607 E. Sonterra Boulevard, San Antonio, TX).)

10. Quest offers for sale and sells cell-free DNA tests that employ methods claimed in the Patents-in-Suit, including the QNatal Advanced test, throughout the United States, including through its website, which is accessible in this District. (*See, e.g.*, Ex. 15 (https://www.questdiagnostics.com/home/physicians/testing-services/by-test-name/noninvasive/requisition/); Ex. 16 at 2 (https://www.questdiagnostics.com/home/physicians/testing-services/by-test-name/noninvasive/faq/) ("How do I order QNatal Advanced? . . . contact your sales representative, email a genetic counselor at GENEINFO@QuestDiagnostics.com, or call 1.866.GENE.INFO (1.866.436.3463)."); Ex. 17 (https://www.questdiagnostics.com/dms/Documents/Other/QNatal-Requisition/QNatal%20Requisition.pdf) (physician order form for QNatal Advanced).)

11. Quest has committed acts of direct infringement in this judicial District. For example, on information and belief, Quest commits acts of infringement in this District by offering for sale and selling the performance of infringing methods at Quest's patient collection centers, such as at 3708 Jefferson Street, Suite B, Austin, TX 78731. Specifically, as detailed further

below, Quest offers for sale and sells the obligation to perform the steps of the patented methods by, for example, offering for sale and selling the QNatal Advanced test.

12. Quest is subject to this Court's jurisdiction pursuant to due process and/or the Texas Long Arm Statute due at least to its substantial business in this State and judicial District, including at least regularly doing and soliciting business at its Austin and San Antonio facilities, and engaging in persistent conduct and/or deriving substantial revenue from goods and services provided to customers in the State of Texas, including in the Western District of Texas. For example, Quest conducts business in the District, by at least offering for sale and selling products and services that comprise the performance of the claimed methods of the Patents-in-Suit, including the QNatal Advanced test, including through its websites, which are accessible in this District. In addition, Quest leases and operates patient collection centers in this District that sell, offer for sale, and support products and services that comprise the performance of the claimed methods of the Patents-in-Suit, including at least the QNatal Advanced test.

13. This Court has personal jurisdiction over Quest due, *inter alia*, to its continuous presence in, and systematic contact with, this District and its registration in Texas. Quest has established minimum contacts within the forum such that the exercise of jurisdiction over Quest will not offend traditional notions of fair play and substantial justice.

14. Personal jurisdiction exists over Quest because Quest, directly and/or through subsidiaries or intermediaries, has committed and continues to commit acts of infringement in this District by, among other things, using products and/or services that infringe the Patents-in-Suit, which led to foreseeable harm and injury to Ravgen.

BACKGROUND OF THE INVENTION

15. Dr. Ravinder S. Dhallan is the founder of Ravgen, Inc. and the inventor of several patents in the field of detection of genetic disorders, including chromosomal abnormalities and mutations. Ravgen's mission is to provide state of the art genetic testing that will enrich the lives of its patients. For example, through the use of its novel techniques in non-invasive prenatal diagnostic testing, Ravgen gives patients the knowledge they need to prepare for their pregnancies and treat diseases at an early stage.

16. Prior to founding Ravgen, Dr. Dhallan was a board-certified emergency room physician. During his time at medical school and his residency at Mass General (Harvard University School of Medicine), Dr. Dhallan and his wife suffered three miscarriages. At that time, the prenatal diagnostic testing procedures available included (a) non-invasive techniques with low sensitivity and specificity, and (b) tests with higher sensitivity and specificity that were highly invasive and therefore associated with a risk for loss of pregnancy. After discovering the limitations on the available techniques for prenatal testing, Dr. Dhallan made it his mission to invent an improved prenatal diagnostic exam—one that was both non-invasive and accurate. In September of 2000, Dr. Dhallan founded Ravgen (which stands for "Rapid Analysis of Variations in the GENome") to pursue that goal.

17. Prior to Ravgen's inventions, scientists had recognized the need for a genetic testing technique that used "cell-free" or "free" fetal DNA circulating in maternal blood. A technique that relied on circulating free fetal DNA would require only a simple blood draw from the mother and would therefore be improvement over invasive diagnostic tests.

18. However, at that time, the use of free fetal DNA for detecting chromosomal abnormalities was limited by the low percentage of free fetal DNA that could be recovered from a

sample of maternal blood using existing techniques. (*See, e.g.*, Ex. 18 (Y.M. Dennis Lo et al., *Presence of Fetal DNA in Maternal Plasma and Serum*, 350 THE LANCET 768-75 (1997), https://doi.org/10.1016/S0140-6736(97)02174-0.) Dr. Dhallan recognized that a method that could increase the percentage of free fetal DNA relative to the free maternal DNA in a sample was necessary to the development of an accurate, non-invasive prenatal diagnostic test.

19. After substantial research, Dr. Dhallan conceived that including an agent that impedes cell lysis (disruption of the cell membrane) if cells are present during sample collection, shipping, handling, and processing would permit the recovery of a larger percentage of cell-free fetal DNA (relative to the cell-free maternal DNA in a sample). Dr. Dhallan hypothesized that this new approach would decrease the amount of maternal cell lysis and therefore lower the amount of cell-free maternal DNA in the sample, thereby increasing the percentage of cell-free fetal DNA. He developed a novel method for processing cell-free fetal DNA that involved the addition of an agent that impedes cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—to maternal blood samples coupled with careful processing protocols. With that novel method, Dr. Dhallan was able to increase the relative percentage of cell-free fetal DNA in the processed sample.

20. Having successfully increased the relative percentage of cell-free fetal DNA recovered, Dr. Dhallan next addressed the challenge of distinguishing between the cell-free maternal and cell-free fetal DNA in a sample in order to determine whether a chromosomal abnormality is present in the fetal DNA. Prior to Ravgen's inventions, known methods for detecting fetal chromosomal abnormalities were time-consuming and burdensome. Many required amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product in a sample. Dr. Dhallan developed an alternate method that greatly increased the

efficiency of this process by taking advantage of the variation of base sequences among different individuals (including a mother and fetus) ("alleles") at particular positions ("loci") on chromosomes. The term "allele" refers to an alternate form of a gene, or a non-coding region of DNA that occurs at a particular loci on a chromosome. The alleles present at certain loci on chromosomes (including, for example, "single nucleotide polymorphisms" or "SNPs") vary between different individuals. At such a locus, a fetus may therefore inherit an allele from its father that differs from the alleles present at that locus on its mother's chromosome. Dr. Dhallan developed a novel method for quantifying the allelic ratio at such a locus (or loci) of interest in a sample comprising maternal and fetal cell-free DNA in order to detect whether a fetal chromosomal abnormality was present in the fetal DNA of the sample, without requiring physical separation of the fetal from the maternal cell-free DNA.

21. Dr. Dhallan understood that his breakthroughs laid the foundation for the development of accurate non-invasive prenatal diagnostic tests. For example, he published a paper in the *Journal of the American Medical Association* (*JAMA*) in 2004, explaining that "the methods described herein for increasing the percentage of cell-free fetal DNA provide a solid foundation for the development of a noninvasive prenatal diagnostic test." (Ex. 19 at 1119 (R. Dhallan et al., *Methods to Increase the Percentage of Free Fetal DNA Recovered from the Maternal Circulation*, 291 JAMA 1114–19 (2004), https://doi.org/10.1001/jama.291.9.1114).)

22. *JAMA* also ran an editorial alongside Dr. Dhallan's article in 2004, recognizing the significance of his inventions to applications in prenatal genetic diagnosis and cancer detection and surveillance:

> In this issue of THE JOURNAL, the findings reported in the study by Dhallan and colleagues on enhancing recovery of cell-free DNA in maternal blood have major clinical implications. Developing a reliable, transportable technology for cell-free DNA analysis

> impacts 2 crucial areas—prenatal genetic diagnosis and cancer detection and surveillance. In prenatal genetic diagnosis, detecting a fetal abnormality without an invasive procedure (or with fewer invasive procedures) is a major advantage. Likewise in cancer surveillance (eg, in patients with leukemia), monitoring treatment without having to perform a bone marrow aspiration for karyotype also would be of great benefit.
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> * * *
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> With prospective studies focusing on clinical applications of these findings, profound clinical implications could emerge for prenatal diagnosis and cancer surveillance.

(Ex. 20 at 1135, 1137 (J.L. Simpson & F. Bischoff, *Cell-Free Fetal DNA in Maternal Blood: Evolving Clinical Applications*, 291 JAMA 1135–37 (2004), https://doi.org/10.1001/jama.291.9.1135).)

23. In 2007, Dr. Dhallan published a second journal article in *The Lancet* that presented a study showcasing Ravgen's ability to use its novel technology to detect Down's syndrome using free fetal DNA in a maternal blood sample. (Ex. 21 (R. Dhallan et al., *A Non-Invasive Test for Prenatal Diagnosis Based on Fetal DNA Present in Maternal Blood: A Preliminary Study*, 369 THE LANCET 474–81 (2007), https://doi.org/10.1016/S0140-6736(07)60115-9).) Dr. Dhallan's peers at *The Lancet* also recognized that his innovative test "opens a new era in prenatal screening." (*See* Ex. 22 (A. Benachi & J.M. Costa, *Non-Invasive Prenatal Diagnosis of Fetal Aneuploidies*, 369 THE LANCET 440–42 (2007), https://doi.org/10.1016/S0140-6736(07)60116-0).)

24. Dr. Dhallan's publications received worldwide press coverage, from outlets such as CNN, BBC, and Washington Post. (*See* Ex. 23 (L. Palmer, *A Better Prenatal Test?*, CNN MONEY (Sept. 12, 2007), https://money.cnn.com/2007/09/07/smbusiness/amniocentesis.fsb/index.htm); Ex. 24 (*Hope for Safe Prenatal Gene Test*, BBC NEWS, Feb 2, 2007, http://news.bbc.co.uk/2/hi/health/6320273.stm); Ex. 25 (A. Gardner, *Experimental Prenatal Test*

Helps Spot Birth Defects, WASH. POST (Feb. 2, 2007), https://www.washingtonpost.com/wp-dyn/content/article/2007/02/02/AR2007020200914.html).)

25. The Patents-in-Suit resulted from Dr. Dhallan's years-long research at Ravgen to develop these innovative new methods for detecting genetic disorders.

PATENTS-IN-SUIT

26. Ravgen incorporates by reference paragraphs 1–25.

27. The '277 Patent, entitled "Methods For Detection Of Genetic Disorders," was duly and legally issued by the United States Patent and Trademark Office on February 19, 2008. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the '277 Patent is attached hereto as Exhibit 1.

28. Ravgen is the exclusive owner of all rights, title, and interest in the '277 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the '277 Patent. (*See* Ex. 3.)

29. The '720 Patent, entitled "Methods For Detection Of Genetic Disorders," was duly and legally issued by the United States Patent and Trademark Office on June 1, 2010. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the '720 Patent is attached hereto as Exhibit 2.

30. Ravgen is the exclusive owner of all rights, title, and interest in the '720 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the '720 Patent. (*See* Ex. 4.)

31. The '277 Patent is directed to, among other things, novel methods used in the detection of genetic disorders. For example, claim 81 of the '277 Patent recites:

> A method for preparing a sample for analysis comprising isolating free fetal nucleic acid from a the sample, wherein said sample

> comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor.

32. The '720 Patent is directed to novel methods for detecting a free nucleic acid in a sample. For example, claim 1 of the '720 Patent recites:

> A method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; and (b) detecting the presence or absence of the free nucleic acid.

33. The Patents-in-Suit are directed to unconventional, non-routine techniques for preparing and analyzing extracellular circulatory DNA, including for the detection of genetic disorders. The Patents-in-Suit explain that, *inter alia*, the inventions claimed therein overcame problems in the field—for example, that the low percentage of fetal DNA in maternal plasma makes using the DNA for genotyping the fetus difficult—with a novel and innovative solution—the addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample, which increase the percentage of cell-free DNA available for detection and analysis:

> The percentage of fetal DNA in maternal plasma is between 0.39-11.9% (Pertl, and Bianchi, *Obstetrics and Gynecology* 98: 483-490 (2001)). **The majority of the DNA in the plasma sample is maternal, which makes using the DNA for genotyping the fetus difficult**. However, methods that increase the percentage of fetal DNA in the maternal plasma allow the sequence of the fetal DNA to be determined, and allow for the detection of genetic disorders including mutations, insertions, deletions, and chromosomal abnormalities. **The addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample can increase the relative percentage of fetal DNA.** While lysis of both maternal and fetal cells is inhibited, the vast majority of cells are maternal, and thus by reducing the lysis of maternal cells, there is a relative increase in the percentage of free fetal DNA.

(Ex. 1 ('277 Patent) at 32:24–39; Ex. 2 ('720 Patent) at 33:31–46 (emphases added).)

34. The Patents-in-Suit teach that the benefit of Dr. Dhallan's discovery, an increase in the relative percentage of cell-free DNA, is realized by performance of the claimed method, including through the inclusion of an agent that inhibits the lysis of the cells in a sample:

> An overall increase in fetal DNA was achieved by reducing the maternal cell lysis, and thus, reducing the amount of maternal DNA present in the sample. In this example, formaldehyde was used to prevent lysis of the cells, however any agent that prevents the lysis of cells or increases the structural integrity of the cells can be used. The increase in fetal DNA in the maternal plasma allows the sequence of the fetal DNA to be determined, and provides for the rapid detection of abnormal DNA sequences or chromosomal abnormalities including but not limited to point mutation, reading frame shift, transition, transversion, addition, insertion, deletion, addition-deletion, frame-shift, missense, reverse mutation, and microsatellite alteration, trisomy, monosomy, other aneuploidies, amplification, rearrangement, translocation, transversion, deletion, addition, amplification, fragment, translocation, and rearrangement.

(Ex. 1 ('277 Patent) at 91:44–60; Ex. 2 ('720 Patent) at 92:10–26.)

35. For example, during the prosecution of the '720 Patent at the Patent and Trademark Office, Ravgen explained that the innovative concept of using agents that inhibit cell lysis during cell-free DNA detection and analysis is recited by the claimed methods of the '720 Patent, including in claim 1:

> Applicant has discovered that the addition of a cell lysis inhibitor to a sample prior to detecting the presence of free nucleic acid can ***significantly and unexpectedly*** increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample.
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> * * *
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> The methods disclosed in claims 1-8, 21-23, and 26 serve a long-felt need in the medical community, and provide unexpected results, and are therefore non-obvious.

(Ex. 5 ('720 File History, June 2, 2009 Response to Office Action) at 12, 14 (emphasis added).)

36. The inventive concept of the Patents-in-Suit of including an agent that inhibits cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—with a

sample represented a significant improvement in the preparation of samples used for non-invasive testing, including non-invasive prenatal testing to unmask previously undetectable fetal genetic traits. At the time of the invention, it would not have been routine or conventional to add an agent that inhibits cell lysis to a sample to increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample. In fact, as described above, that inventive concept was recognized by Dr. Dhallan's peers as "an important step in improving detection of cell-free DNA." (Ex. 20 at 1137.)

37. The '277 Patent is further directed to an unconventional, non-routine method of detecting fetal chromosomal abnormalities which involves "quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA." (Ex. 26 ('277 File History, May 30, 2007 Response to Office Action) at 30.) For example, claim 1 of the '277 Patent recites:

> A method for detecting the presence or absence of a fetal chromosomal abnormality, said method comprising: quantitating a ratio of the relative amounts of alleles at a heterozygous locus of interest in a mixture of template DNA, wherein said mixture comprises maternal DNA and fetal DNA, and wherein said mixture of maternal DNA and fetal DNA has been obtained from a sample from a pregnant female, and further wherein said heterozygous locus of interest has been identified by determining the sequence of alleles at the locus of interest, and wherein said ratio indicates the presence or absence of a fetal chromosomal abnormality.

38. The '277 Patent explains that this claimed method represented a significant improvement over prior art methods of detecting fetal chromosomal abnormalities, many of which were costly, time-consuming, and burdensome because they either required the amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product. (Ex. 1 at 66:14-20.) By contrast, the claimed "ratio" method of the '277 Patent only requires sequencing of discrete "loci of interest" (such as "single nucleotide polymorphisms," or "SNPs") from the collected DNA sample. (*Id.* at 34:63-35:37 ("In fact, it is an advantage of the invention

that primers that copy an entire gene sequence need not be utilized. . . . There is no advantage to sequencing the entire gene as this can increase cost and delay results. Sequencing only the desired bases or loci of interest maximizes the overall efficiency of the method because it allows for the sequence of the maximum number of loci of interest to be determined in the fastest amount of time and with minimal cost." *Id.* at 35:28-37.).)

39. During the prosecution of the '277 Patent at the Patent and Trademark Office, Ravgen gave the following example of an implementation of the claimed "ratio" method:

> Applicants have invented a method for detecting the presence or absence of a fetal chromosomal abnormality, wherein the method comprises, inter alia, quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA.
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> ***
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> [R]atios were calculated at both chromosomes 13 and 21 in a heterogeneous mixture of 75% Down syndrome DNA and 25% maternal DNA. Single nucleotide polymorphisms were analyzed wherein the maternal genome was homozygous for one allele at a specific genetic site and the Down syndrome DNA was heterozygous at the same genetic site. If at a certain site, the maternal genome contains an adenine at both copies of chromosome 13, and the Down syndrome genome is comprised of one chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.60 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.25 + 0.25 maternal A alleles).
>
> On the other hand, if at a certain genetic site on chromosome 21, the maternal genome contains an adenine at both copies of chromosome 21, and the Down syndrome genome is comprised of two chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.375 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.75 Down syndrome A allele + 0.25 + 0.25 (maternal A alleles). Thus, the methods described in the present application detect chromosomal abnormalities using a method that comprises, inter alia, quantitating a ratio of alleles in a heterogeneous mixture of DNA, wherein the ratio represents alleles from more than one individual.

(Ex. 26 at 30.)

QUEST'S INFRINGING ACTIVITIES

(The Accused QNatal Advanced Test)

40. Ravgen incorporates by reference paragraphs 1–39.

41. On May 12, 2015, Quest launched the QNatal Advanced test, a commercial non-invasive prenatal test for detecting fetal genetic abnormalities. (*See* Ex. 27 at 1 (Press Release, Quest Diagnostics to Enhance Quality of Noninvasive Prenatal Screening with QNatal Advanced (May 12, 2015), https://newsroom.questdiagnostics.com/2015-05-12-Quest-Diagnostics-to-Enhance-Quality-of-Noninvasive-Prenatal-Screening-with-QNatal-Advanced) ("Quest Diagnostics (NYSE: DGX), the world's leading provider of diagnostic information services and a leader in women's health and genomic testing, today launched QNatal Advanced, a noninvasive prenatal screening service for detecting chromosomal abnormalities in high-risk pregnancies.").)

42. The QNatal Advanced test "analyzes cell-free fetal DNA in circulating maternal blood." (*Id.*; *see also* Ex. 28 at 1 (http://education.questdiagnostics.com/faq/FAQ167) ("The QNatal Advanced test is performed on cell-free DNA (cfDNA) isolated from maternal blood.").)

43. Quest offers to sell and sells the QNatal Advanced test on its website and at its patient collection centers, including several patient collection centers in this District (such as at 3708 Jefferson Street, Suite B, Austin, TX 78731). (*See* Ex. 8 at 1; Ex. 15-16; Ex. 29 at 2 (Quest Diagnostics Incorporated, *QNatal Advanced Noninvasive Prenatal Screening: Screening for the Health of Your Baby* (2019), https://fenwayhealth.org/wp-content/uploads/QNatal-Advanced-Screening-Patient-Brochure.pdf).) On information and belief, Quest's offers for sale and sales of the QNatal Advanced test comprise the obligation to perform the steps of the infringing methods. For example, when a patient is referred by her healthcare provider to visit a Quest patient service center, and she agrees to pay (or for her insurer to pay) in exchange for the QNatal Advanced test,

on information and belief, Quest accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the QNatal Advanced test protocol for the patient's sample(s). At these centers, Quest collects test samples from patients, including pregnant women, for the QNatal Advanced test. (*See* Ex. 29 at 2 ("How is QNatal Advanced performed? QNatal Advanced is a simple blood draw. . . . You can have the test performed at . . . your local Quest Diagnostics Patient Service Center.").) On information and belief, employees or other agents of Quest (e.g., Quest's phlebotomists) collect test samples according to the QNatal Advanced test protocol.

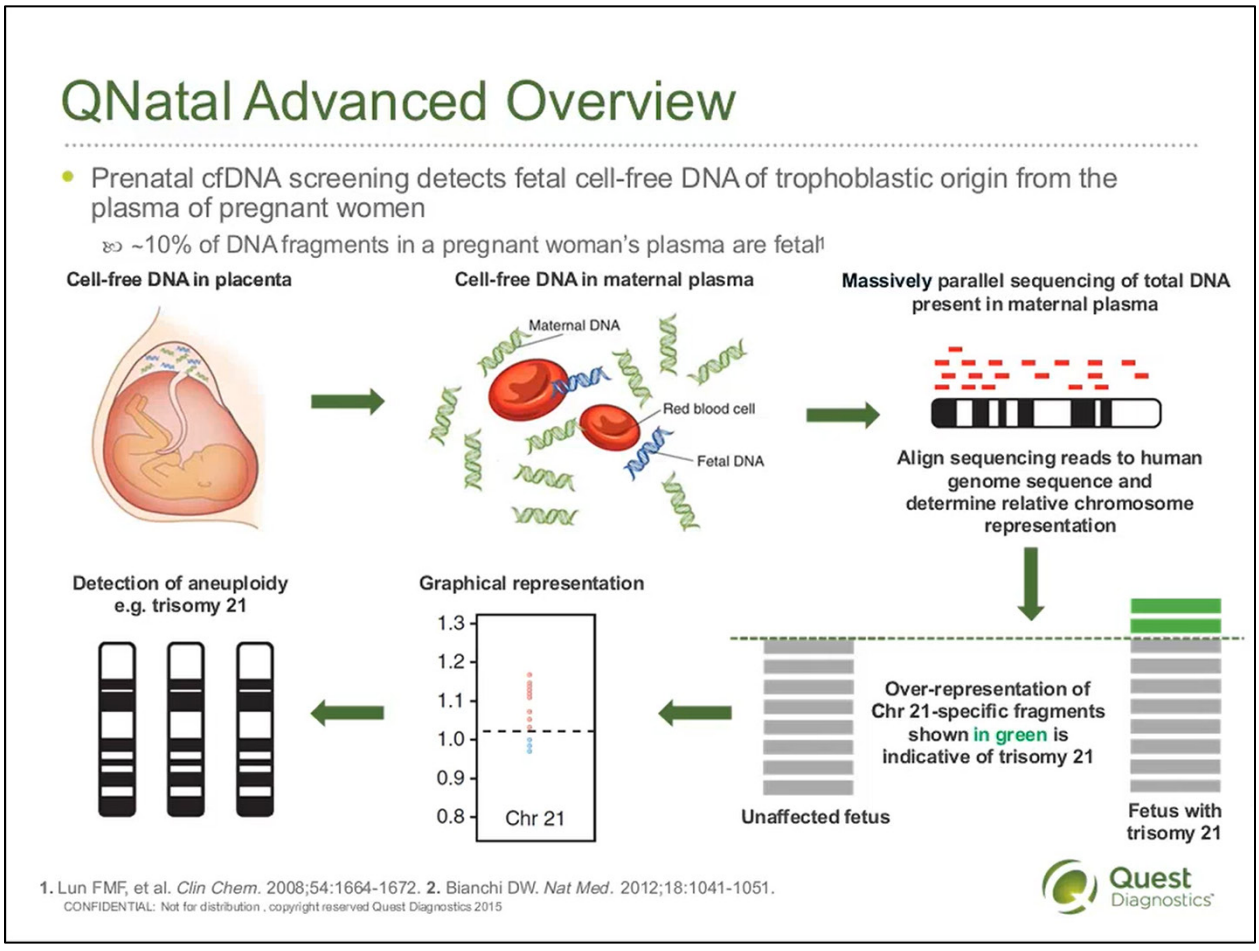
44. Quest publishes and follows Test Details for the QNatal Advanced test, which include instructions for collecting and transporting test samples. (*See* Ex. 30 (https://testdirectory.questdiagnostics.com/test/test-detail/92777/qnatal-advanced?cc=DAL).) On information and belief, the published Test Details are a part of the QNatal Advanced test protocol, and Quest directs its employees and other agents to follow the QNatal Advanced test protocol.

45. The QNatal Advanced test requires samples containing an agent that inhibits cell lysis. For example, in the QNatal Advanced Test Details, Quest provides the following Collection Instructions: "Use Streck tubes only. Volume 20mL (16 mL minimum) whole blood collected in two Streck cell-free (black/tan tiger-top) tubes (10 mL in each tube)," and Quest specifies that samples must be transported in "Cell-free DNA Streck tubes." (Ex. 30 at 1 (https://testdirectory.questdiagnostics.com/test/test-detail/92777/qnatal-advanced?cc=DAL).) Quest also indicates that the "Preferred Specimen" for the QNatal Advanced test is "10 mL whole blood collected in each of two separate Streck cell-free (black/tan tiger-top) glass tubes." (*Id.*)

46. The Streck Cell-Free DNA Blood Collection Tube ("BCT") includes an agent that inhibits cell lysis. A Streck Cell-Free DNA BCT "stabilizes nucleated blood cells. The unique

preservative ***limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA***. Cell-Free DNA BCT has also been demonstrated to minimize the degradation of circulating tumor cells (CTCs). By ***limiting cell lysis***, the specialized chemistry provides sample integrity during storage, shipping and handling of blood samples. Cell-free DNA and gDNA are stable for up to 14 days at 6 °C to 37 °C. CTCs are stable for up to 7 days at 15 °C to 30 °C." (Ex. 31 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources).)

47. In processing QNatal Advanced tests, Quest isolates cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT and then analyzes the isolated fetal cell-free DNA to detect chromosomal abnormalities as shown below:



(Ex. 32 ("Prenatal Genetic Screening: Simplifying Test Selection in the Age of Expanding Options," https://education.questdiagnostics.com/presentations/prenatal-genetic-screening-simplifying-test-selection-in-the-age-of-expanding-options?presentation_id=371), slide at 15:27; *see also id.*, video at 15:05-16:34 ("When we analyze the cfDNA, we're actually analyzing it all together, both maternal and fetal all in combination with each other, and then the next-generation sequencing after the cfDNA is detected and amplified, it can actually rearrange those fragments to the chromosomes of origin that they originated from, and this is a bioinformatics process. And so, once a number of sequence reads have been arranged to the chromosome of origin, that is when you can understand whether there seems to be an overrepresentation of sequence reads. So you can see here that we have a rudimentary bar graph demonstrating this concept, where we would expect to have a certain number of sequence reads from an unaffected fetus and mother of chromosome 21, and when we see an overrepresentation of sequence reads or cfDNA from a fetus with trisomy 21, you will see basically, as I said, an overrepresentation over what is expected, and then deductive reasoning can be used to say, if there are increased sequenced reads from this chromosome, the logical explanation for those increases, those reads being there, is that there is an extra chromosome present, and that is how the calls are made between an unaffected fetus and a fetus that is infected with trisomy. These sequence reads are then translated into a z-score, which is more or less a representation of how far away, how many standard deviations away you are from the expected median or average . . ." (narration)); *see also* Ex. 28 at 1 ("The QNatal Advanced test is performed on cell-free DNA (cfDNA) isolated from maternal blood. This cfDNA contains both maternal DNA and fetal DNA derived from apoptotic placental cells (trophoblasts). Once isolated, the cfDNA is sequenced using massively parallel shotgun sequencing (MPSS); this is followed by

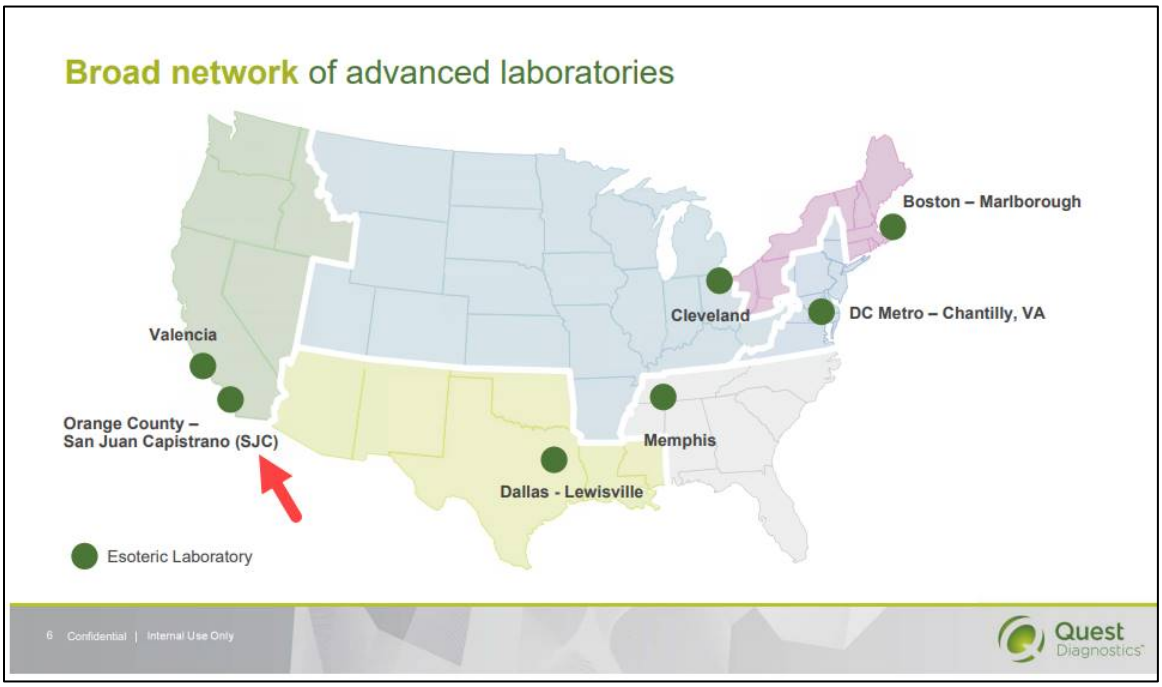
quantitative bioinformatics analysis. In this way, the fetal copy number of chromosomes 21, 18, 13, X, Y and select microdeletion regions are calculated.").)

48. Quest processes the QNatal Advanced test samples at its subsidiary laboratory, Quest Diagnostics Nichols Institute ("Quest Nichols"). (Ex. 30 at 3 (https://testdirectory.questdiagnostics.com/test/test-detail/92777/qnatal-advanced?cc=DAL) ("Performing Laboratory: Quest Diagnostics Nichols Institute-San Juan Capistrano, CA").) On information and belief, Quest Nichols operates as Quest's laboratory and carries out Quest's business. Through Quest Nichols, Quest develops and processes several of its diagnostic tests, including the QNatal Advanced test. On information and belief, Quest instructs Quest Nichols to processes the collected samples in accordance with the established QNatal Advanced test protocol. On information and belief, Quest conditions participation in an activity or receipt of a benefit (such as continued funding, status as Quest's laboratory, and payments related to discrete tests performed) on Quest Nichols's processing of the QNatal Advanced test samples.

49. Quest's SEC filings demonstrate that Quest Nichols operates as Quest's laboratory, and that Quest authorizes Quest Nichols to act on its behalf. For example, Quest states in its Form 10-K for fiscal year 2019: "We offer the broadest access in the United States to clinical testing. We maintain a nationwide network of laboratories, including advanced laboratories (such as our world-renowned Quest Diagnostics Nichols Institute) . . . ." (Ex. 7 at 11.) As another example, Quest stated in its Form 10-K for fiscal year 2015: "We are a leading innovator in diagnostic information services with outstanding medical and technical expertise. We continue to introduce new tests and services, including many with a focus on personalized and targeted medicine. Our capabilities include early discovery, technology development and clinical validation of diagnostic tests. We develop tests at our laboratories, such as Quest Diagnostics Nichols Institute and Athena

Diagnostics. . . . We conduct complex and specialized testing, including molecular diagnostics, in our world renowned Quest Diagnostics Nichols Institute laboratory facilities . . . ." (Ex. 33 at 5, 8.) Quest's SEC filings further confirm that at all relevant times, Quest Diagnostics Incorporated owned and owns 100% of Quest Diagnostics Nichols Institute, and that Quest has the right and the ability to direct and control the activities of Quest Nichols. (*E.g.*, Ex. 7 at Exhibit 21.1 ("Subsidiaries, Joint Ventures and Affiliates" on Form 10-K).) Further, Quest's SEC filings, such as the portions quoted above, show that Quest consents for Quest Nichols to act on Quest's behalf, including to perform tests on Quest's behalf and provide results to health care providers and/or patients on Quest's behalf.

50. In its marketing materials, Quest identifies Quest Nichols (located in San Juan Capistrano) as one of Quest's "advanced laboratories":



(Ex. 34 at 6 (https://s2.q4cdn.com/390454341/files/doc_presentations/4_Innovation-and-Growth-in-ADx-Carrie-Eglinton-Manner-safe-harbor.pdf) (annotation added).)

51. Quest is the "Owner" of Quest Nichols on Quest Nichols's California laboratory license:

CDPH California Department of PublicHealth

CLINICAL AND PUBLIC HEALTH LABORATORY LICENSE

In accordance with the provisions of Chapter 3, Division 2 of the Business and Professions Code, the persons named below are hereby issued a license authorizing operation of a clinical laboratory at the indicated address.

QUEST DIAGNOSTICS NICHOLS INSTITUTE

33608 ORTEGA HIGHWAY,
SAN JUAN CAPISTRANO, CA 92690-6130

STATE ID: CDF-00002562
SCAN QR CODE TO VERIFY LICENSE
OR VISIT: www.cdph.ca.gov/LFS
EFFECTIVE DATE: 12/29/2019
EXPIRATION DATE: 12/28/2020

LICENSE TYPE:
CLINICAL LABORATORY LICENSE
CERTIFICATE OF DEEMED STATUS
CLIA ID: 05D0643352

OWNER/S:
QUEST DIAGNOSTICS, INC. (DE)

DIRECTOR/S:
MARAMICA, IRINA,
LACBAWAN, FELICITAS, L

DISPLAY: State law requires that the clinical laboratory license shall be conspicuously posted in the clinical laboratory.
CHANGE OF LABORATORY NAME, DIRECTOR, OWNER AND/OR ADDRESS:
State law requires that the laboratory owner and/or the director notify this office within 30 days of any change in ownership, name, location, or laboratory directors.
YOUR LICENSE MAY BE REVOKED 30 DAYS AFTER A MAJOR OWNER AND/OR DIRECTOR CHANGE.
If your license is revoked, you must cease engaging in clinical laboratory practice and apply for a new clinical laboratory license.
To make these changes or to submit a new application, visit our website: https://www.cdph.ca.gov/LFS *(Go to Clinical Laboratory Facilities)*

Robert J. Thomas
ROBERT J. THOMAS
BRANCH CHIEF
LABORATORY FIELD SERVICES

LABCERT 300 (05-2019)

(Ex. 35 (https://www.questdiagnostics.com/dms/Documents/Other/CLIA_Certificates/Licenses-Acccreditations/EZ_SJC-QDNI/EZ_California.pdf) (annotation added).)

52. Additionally, Quest represents in its press releases that Quest directs and controls the diagnostic test development and processing of Quest Nichols, such that Quest Nichols is Quest's laboratory, and the two operate as one integrated business. For example, press releases related to the launch of the QNatal Advanced test represent that Quest developed the test: "Quest Diagnostics (NYSE: DGX), the world's leading provider of diagnostic information services and a leader in women's health and genomic testing, today launched QNatal Advanced. . . . 'With QNatal Advanced, Quest Diagnostics is delivering on its commitment to provide clinically important

innovations aligned with guideline-based care as part of a full range of capabilities that support a woman through her pregnancy,' said Charles ('Buck') Strom, MD, PhD, vice president, genomics and genetics, Quest Diagnostics." (Ex. 36 at 1 (https://newsroom.questdiagnostics.com/2015-05-12-Quest-Diagnostics-to-Enhance-Quality-of-Noninvasive-Prenatal-Screening-with-QNatal-Advanced).) "NYSE: DGX" is the stock ticker of Quest Diagnostics Incorporated. (*See, e.g.*, Ex. 7 at 40; Ex. 37 at 1 (https://s2.q4cdn.com/390454341/files/doc_news/archive/c132b3e8-4eb9-4e87-9d75-58bd16f735c2.pdf).) As another example, press releases describe Quest Nichols as the laboratory of Quest, and as "Quest Diagnostics' Center for Diagnostic Innovation": "In his new role, Dr. Cooper will manage reference laboratory operations for Quest Diagnostics' San Juan Capistrano-based facility, oversee research and development activities, and supervise business administration functions at Nichols Institute. . . . Dr. Cooper's expertise and leadership in the field of molecular diagnostics square position Nichols Institute as Quest Diagnostics' Center for Diagnostic Innovation . . . This signals our commitment to the growth of molecular medicine in health care, and the provision of the most technologically-advanced diagnostic and prognostic testing services in a commercial reference laboratory environment." (Ex. 38 (https://s2.q4cdn.com/390454341/files/doc_news/archive/31624b9d-00c4-4a05-937e-41a87d68edef.pdf) (citations omitted).)

53. Quest also pays for the legal fees for Quest Nichols, including the cost of a 2001 legal settlement in a case filed against Quest Nichols. (*See* Ex. 37 (Press Release, Quest Diagnostics Resolves Government Claims Against Nichols Institute (Jan. 3, 2001), https://s2.q4cdn.com/390454341/files/doc_news/archive/c132b3e8-4eb9-4e87-9d75-58bd16f735c2.pdf) ("Quest Diagnostics Incorporated (NYSE: DGX), the nation's leading provider of diagnostic testing, information and services, announced that it has agreed to refund

$13.08 million to federal and certain state government health care programs. This resolves previously disclosed claims related to certain billing and marketing practices at several former facilities of the company's Nichols Institute unit that occurred prior to its acquisition by Corning Incorporated, the former parent of Quest Diagnostics, in 1994. . . . The government claimed that Nichols Institute routine testing laboratories located in five states performed and billed certain laboratory tests, included in certain groupings of tests that were ordered for patients by physicians, which the government subsequently considered to be 'medically unnecessary.' Quest Diagnostics had an active compliance program at the time Nichols Institute was acquired and instituted programs and measures to conform Nichols Institute's practices with the company's understanding of legal and regulatory requirements and policies").) Based at least on Quest's statements asserting that Quest "instituted programs and measures to conform Nichols Institute's practices with the company's [i.e., Quest Diagnostics Incorporated's] understanding" (*id.*), Quest has exercised its right and ability to direct and control Quest Nichols's operations, and both entities understand that Quest Nichols consents to act subject to Quest's control.

54. Quest also indicates on its website that "Nichols Institute" is a registered trademark of Quest:

(*E.g.*, Ex. 39.)

55. Additionally, at least some members of the Quest "Management Team" work at Quest Nichols. For example, Jay G. Wohlgemuth, M.D. is Senior Vice President, R&D, Medical and Chief Medical Officer for Quest, and also works at Quest Nichols. (Ex. 40 at 2 (https://ir.questdiagnostics.com/governance/management-team/default.aspx) ("Based in Quest Diagnostics Nichols Institute, in San Juan Capistrano, California, Dr. Wohlgemuth is responsible

for Research & Development, Medical Affairs, and Medical/Lab Quality.").) On information and belief, Dr. Wohlgemuth is an employee and/or officer of Quest, whose leadership position at Quest Nichols further enables Quest to exercise direction and control over the activities of its fully owned subsidiary, Quest Nichols.

56. Quest informs patients that the QNatal Advanced test is "developed and performed exclusively by Quest Diagnostics":

QNatal Advanced noninvasive prenatal screen is a laboratory-developed test, developed and performed exclusively by Quest Diagnostics. It has not been cleared or approved by the US Food and Drug Administration (FDA). Although laboratory-developed tests to date have not been subject to US FDA regulation, certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. QNatal Advanced is performed exclusively by Quest Diagnostics.

QuestDiagnostics.com

Quest Diagnostics Incorporated and its subsidiaries (Quest) complies with applicable federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. ATTENTION: If you speak **English**, language assistance services, free of charge, are available to you. Call 1.844.698.1022. ATENCIÓN: Si habla **español (Spanish)**, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.844.698.1022. 注意：如果您使用繁體中文 **(Chinese)**, 您可以免費獲得語言援助服務. 請致電 1.844.698.1022.

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Quest Diagnostics™

(Ex. 29 at 1.)

COUNT I

(Infringement Of The '277 Patent)

57. Ravgen incorporates by reference paragraphs 1–56.

58. The '277 Patent is valid and enforceable.

59. Quest has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including Quest's QNatal Advanced test.

60. For example, Quest infringes at least exemplary claim 81 of the '277 Patent by using the QNatal Advanced test. For example, use of the QNatal Advanced test requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 28 at 1 (describing isolating cell-free fetal DNA from a maternal blood sample)),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of blood) (*see, e.g.*, Ex. 30 at 1 (describing that the QNatal Advanced test requires "[v]olume 20mL (16 mL minimum) whole blood collected in two Streck cell-free (black/tan tiger-top) tubes (10 mL in each tube)")); Ex. 31 at 2 (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

61. Quest has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the QNatal Advanced test either itself or through its agent, Quest Nichols. For example, Quest assigns its laboratory Quest Nichols the task of using the QNatal Advanced test (by collecting

samples and sending them to Quest Nichols for processing), and Quest gives interim instructions to control the means and details of the process by which Quest Nichols uses the QNatal Advanced tests (by establishing the QNatal Advanced test protocol and requiring Quest Nichols to follow that protocol when processing tests). Quest has the right and the ability to direct and control the activities of Quest Nichols in several ways, including through Quest's 100% ownership of Quest Nichols, through instituting programs and measures (such as policies or protocols) at Quest Nichols, and through interim instructions via at least Quest's employees and/or officers who hold leadership roles at Quest Nichols. Further, Quest Nichols acts on behalf of Quest, including when Quest Nichols performs tests on Quest's behalf for Quest's patients, or provides test results to health care providers and/or patients on Quest's behalf.

62. Quest has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the QNatal Advanced test, comprising the performance of the patented methods, by its laboratory Quest Nichols. For example, Quest conditions participation in an activity or receipt of a benefit (such as continued funding and status as Quest's laboratory) on Quest Nichols's performance of the steps of the patented method (such as the processing of the QNatal Advanced test samples). Further, Quest establishes the manner or timing of the performance of the steps of the patented method (such as Quest Nichols's processing of the QNatal Advanced test samples), including by collecting test samples and sending them to Quest Nichols with instructions to be processed according to the QNatal Advanced test protocol that Quest established, which includes details regarding the sequence of steps to perform and the time frame of "Specimen Viability" within which a sample must be processed after it is collected. On information and belief, employees or other agents of Quest (e.g., Quest's phlebotomists) collect

test samples according to the QNatal Advanced test protocol, and Quest Nichols processes the test samples according to the QNatal Advanced test protocol.

63. Quest has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by offering for sale and selling the performance of infringing methods, such as by offering for sale and selling the QNatal Advanced test. Quest's offers for sale and sales of the QNatal Advanced test comprise the obligation to perform the steps of the patented methods. For example, when a patient agrees to pay (or for her insurer to pay) in exchange for the QNatal Advanced test, on information and belief, Quest accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the QNatal Advanced test protocol for the patient's sample(s), including the acts of collecting a patient sample according to the QNatal Advanced test protocol, preparing such sample for analysis so that it comprises an agent that inhibits lysis of cells, if cells are present, isolating free fetal nucleic acid from the sample, and reporting results to a health care provider and/or the patient.

64. In addition or in the alternative, Quest induces infringement of one or more claims of the '277 Patent under 35 U.S.C. § 271(b). Quest actively, knowingly, and intentionally induces infringement of the '277 Patent by selling or otherwise supplying the QNatal Advanced tests with the knowledge and intent that its laboratory Quest Nichols will use the QNatal Advanced tests supplied by Quest to infringe the '277 Patent; and with the knowledge and intent to encourage and facilitate Quest Nichols's infringement through the dissemination of the QNatal Advanced tests and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the QNatal Advanced tests.

65. Quest specifically intends and is aware that the ordinary and customary use of the QNatal Advanced tests would infringe the '277 Patent. For example, Quest sells and provides the QNatal Advanced tests, which when used in their ordinary and customary manner intended and instructed by Quest, infringe one or more claims of the '277 Patent, including at least exemplary claim 81. Quest further provides product manuals and other instructional materials that cause the Quest Nichols laboratory to operate the QNatal Advanced tests for their ordinary and customary use. Quest's laboratory Quest Nichols has directly infringed the '277 Patent, including at least exemplary claim 81, through the normal and customary use of the QNatal Advanced tests. Quest accordingly induces Quest's laboratory Quest Nichols to use the QNatal Advanced tests in their ordinary and customary way to infringe the '277 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '277 Patent.

66. In addition or in the alternative, Quest contributes to the infringement by third parties, including Quest's laboratory Quest Nichols, of one or more claims of the '277 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, the QNatal Advanced tests, knowing that those products constitute a material part of the inventions of the '277 Patent, knowing that those products are especially made or adapted to infringe the '277 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

67. Quest has had knowledge of and notice of the '277 Patent and its infringement since at least the filing of this Complaint.

68. Quest's infringement of the '277 Patent continues to be, willful and deliberate since, at least the filing of this Complaint.

69. Ravgen has been and continues to be damaged by Quest's infringement of the '277 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

70. Quest's conduct in infringing the '277 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

COUNT II

Infringement Of The '720 Patent

71. Ravgen incorporates by reference paragraphs 1–70.

72. The '720 Patent is valid and enforceable.

73. Quest has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including Quest's QNatal Advanced test.

74. For example, Quest infringes at least exemplary claim 1 of the '720 patent by using the QNatal Advanced test. For example, use of the QNatal Advanced test requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as cell-free DNA) from a non-cellular fraction of a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 28 at 1 (describing isolating cell-free fetal DNA from a maternal blood sample)),

b. wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of maternal blood) (*see, e.g.*, Ex. 30 at 1 (describing that the QNatal Advanced test requires "[v]olume 20mL (16 mL minimum) whole blood

collected in two Streck cell-free (black/tan tiger-top) tubes (10 mL in each tube)")); Ex. 31 at 2 (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

c. detecting the presence or absence of the free nucleic acid (*see, e.g.*, Ex. 28 at 1 ("Once isolated, the cfDNA is sequenced using massively parallel shotgun sequencing (MPSS); this is followed by quantitative bioinformatics analysis. In this way, the fetal copy number of chromosomes 21, 18, 13, X, Y and select microdeletion regions are calculated."))

75. Quest has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the QNatal Advanced test either itself or through its agent, Quest Nichols. For example, Quest assigns its laboratory Quest Nichols the task of using the QNatal Advanced test (by collecting samples and sending them to Quest Nichols for processing), and Quest gives interim instructions to control the means and details of the process by which Quest Nichols uses the QNatal Advanced tests (by establishing the QNatal Advanced test protocol and requiring Quest Nichols to follow that protocol when processing tests). Quest has the right and the ability to direct and control the activities of Quest Nichols in several ways, including through Quest's 100% ownership of Quest Nichols, through instituting programs and measures (such as policies or protocols) at Quest Nichols, and through interim instructions via at least Quest's employees and/or officers who hold leadership roles at Quest Nichols. Further, Quest Nichols acts on behalf of Quest, including when Quest Nichols performs tests on Quest's behalf for Quest's patients, or provides test results to health care providers and/or patients on Quest's behalf.

76. Quest has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the QNatal Advanced test, comprising the performance of the patented methods, by its laboratory Quest Nichols. For example, Quest conditions participation in an activity or receipt of a benefit (such as continued funding and status as Quest's laboratory) on Quest Nichols's performance of the steps of the patented method (such as the processing of the QNatal Advanced test samples). Further, Quest establishes the manner or timing of the performance of the steps of the patented method (such as Quest Nichols's processing of the QNatal Advanced test samples), including by collecting test samples and sending them to Quest Nichols with instructions to be processed according to the QNatal Advanced test protocol that Quest established, which includes details regarding the sequence of steps to perform and the time frame of "Specimen Viability" within which a sample must be processed after it is collected. On information and belief, employees or other agents of Quest (e.g., Quest's phlebotomists) collect test samples according to the QNatal Advanced test protocol, and Quest Nichols processes the test samples according to the QNatal Advanced test protocol.

77. Quest has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by offering to sell, and selling the performance of infringing methods, such as by offering for sale and selling the QNatal Advanced test. Quest's offers for sale and sales of the QNatal Advanced test comprise the obligation to perform the steps of the patented methods. For example, when a patient agrees to pay (or for her insurer to pay) in exchange for the QNatal Advanced test, on information and belief, Quest accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the QNatal Advanced test protocol for the patient's

sample(s), including the acts of collecting a patient sample according to the QNatal Advanced test protocol; preparing such sample for analysis so that it comprises an agent that impedes cell lysis, if cells are present, wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; isolating free nucleic acid from a non-cellular fraction of a sample; detecting the presence or absence of the free nucleic acid; and reporting results to a health care provider and/or the patient.

78. In addition or in the alternative, Quest induces infringement of one or more claims of the ’720 Patent under 35 U.S.C. § 271(b). Quest actively, knowingly, and intentionally induces infringement of the ’720 Patent by selling or otherwise supplying the QNatal Advanced tests with the knowledge and intent that its laboratory Quest Nichols will use the QNatal Advanced tests supplied by Quest to infringe the ’720 Patent; and with the knowledge and intent to encourage and facilitate Quest Nichols’s infringement through the dissemination of the QNatal Advanced tests and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the QNatal Advanced tests.

79. Quest specifically intends and is aware that the ordinary and customary use of the QNatal Advanced tests would infringe the ’720 Patent. For example, Quest sells and provides the QNatal Advanced tests, which when used in their ordinary and customary manner intended and instructed by Quest, infringe one or more claims of the ’720 Patent, including at least exemplary claim 1. Quest further provides product manuals and other instructional materials that cause the Quest Nichols laboratory to operate the QNatal Advanced tests for their ordinary and customary use. Quest’s laboratory Quest Nichols has directly infringed the ’720 Patent, including at least exemplary claim 1, through the normal and customary use of the QNatal Advanced tests. Quest accordingly induces Quest’s laboratory Quest Nichols to use the QNatal Advanced tests in their

ordinary and customary way to infringe the '720 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '720 Patent.

80. In addition or in the alternative, Quest contributes to the infringement by third parties, including Quest's laboratory Quest Nichols, of one or more claims of the '720 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, the QNatal Advanced tests, knowing that those products constitute a material part of the inventions of the '720 Patent, knowing that those products are especially made or adapted to infringe the '720 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

81. Quest has had knowledge of and notice of the '720 Patent and its infringement since at least the filing of this Complaint.

82. Quest's infringement of the '720 Patent continues to be, willful and deliberate since, at least the filing of this Complaint.

83. Ravgen has been and continues to be damaged by Quest's infringement of the '720 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

84. Quest's conduct in infringing the '720 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Ravgen prays for judgment as follows:

A. That Quest has infringed each of the Patents-in-Suit;

B. That Quest's infringement of each of the Patents-in-Suit has been willful;

C. That Ravgen be awarded all damages adequate to compensate it for Quest's past infringement and any continuing or future infringement of the Patents-in-Suit up until the date

such judgment is entered, including pre- and post-judgment interest, costs, and disbursements as justified under 35 U.S.C. § 284;

D. That any award of damages be enhanced under 35 U.S.C. § 284 as result of Quest's willful infringement;

E. That this case be declared an exceptional case within the meaning of 35 U.S.C. § 285 and that Ravgen be awarded the attorney fees, costs, and expenses incurred in connection with this action;

F. That Ravgen be awarded either a permanent injunction, or, at least, a compulsory ongoing licensing fee; and

F. That Ravgen be awarded such other and further relief at law or equity as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiff Ravgen hereby demands a trial by jury on all issues so triable.

Dated: October 16, 2020

Respectfully submitted,

/s/ Deron R. Dacus

Deron R. Dacus
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